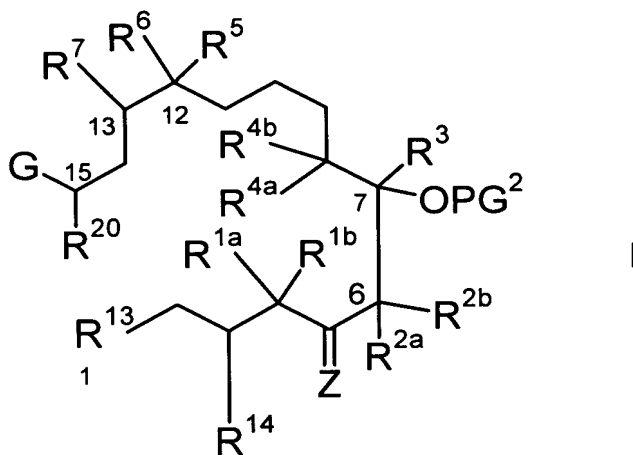


## Claims

1. Process for the production of C<sub>1</sub>-C<sub>15</sub>-epothilone fragments of general formula I,



in which

R<sup>1a</sup>, R<sup>1b</sup> are the same or different and mean hydrogen, C<sub>1</sub>-C<sub>10</sub>-alkyl, aryl,

C<sub>7</sub>-C<sub>20</sub>-aralkyl, or together mean a -(CH<sub>2</sub>)<sub>m</sub> group with m = 2, 3, 4 or 5,

R<sup>2a</sup>, R<sup>2b</sup> are the same or different and mean hydrogen, C<sub>1</sub>-C<sub>10</sub>-alkyl,

C<sub>2</sub>-C<sub>10</sub>-alkenyl, C<sub>2</sub>-C<sub>10</sub>-alkinyl, aryl, C<sub>7</sub>-C<sub>20</sub>-aralkyl or together mean a -(CH<sub>2</sub>)<sub>n</sub> group with n = 2, 3, 4 or 5,

R<sup>3</sup> means hydrogen, C<sub>1</sub>-C<sub>10</sub>-alkyl, aryl, C<sub>7</sub>-C<sub>20</sub>-aralkyl,

R<sup>4a</sup>, R<sup>4b</sup> are the same or different and mean hydrogen, C<sub>1</sub>-C<sub>10</sub>-alkyl, aryl,

C<sub>7</sub>-C<sub>20</sub>-aralkyl or together mean a -(CH<sub>2</sub>)<sub>p</sub> group with p = 2, 3, 4 or 5,

R<sup>5</sup> means hydrogen, C<sub>1</sub>-C<sub>10</sub>-alkyl, aryl, C<sub>7</sub>-C<sub>20</sub>-aralkyl,

$R^6, R^7$  each mean a hydrogen atom, together an additional bond or together an oxygen atom,

G means a group  $X=CR^8$ -, a bicyclic or tricyclic aryl radical,

$R^8$  means hydrogen, halogen,  $C_1$ - $C_{20}$ -alkyl, aryl,  $C_7$ - $C_{20}$ -aralkyl, which all can be substituted,

X means an oxygen atom, two alkoxy groups  $OR^{23}$ , a  $C_2$ - $C_{10}$ -alkylene- $\alpha, \omega$ -dioxy group, which can be straight-chain or branched,  $H/OR^9$  or a grouping  $CR^{10}R^{11}$ ,  
whereby

$R^{23}$  stands for a  $C_1$ - $C_{20}$ -alkyl radical,

$R^9$  stands for hydrogen or a protective group  $PG^X$ ,

$R^{10}, R^{11}$  are the same or different and stand for hydrogen, a  $C_1$ - $C_{20}$ -alkyl, aryl, or  $C_7$ - $C_{20}$ -aralkyl radical, or  $R^{10}$  and  $R^{11}$  together with the methylene carbon atom together stand for a 5- to 7-membered carbocyclic ring,

$R^{13}$  means  $CH_2OR^{13a}$ ,  $CH_2$ -Hal, CHO,  $CO_2R^{13b}$ , or COHal,

$R^{14}$  means hydrogen,  $OR^{14a}$ , Hal, or  $OSO_2R^{14b}$ ,

$R^{13a}, R^{14a}$  mean hydrogen,  $SO_2$ -alkyl,  $SO_2$ -aryl,  $SO_2$ -aralkyl or together a  $-(CH_2)_O$  group or together a  $CR^{15a}R^{15b}$  group,

$R^{13b}, R^{14b}$  mean hydrogen,  $C_1$ - $C_{20}$ -alkyl, aryl,  $C_1$ - $C_{20}$ -aralkyl,

$R^{15a}, R^{15b}$  are the same or different and mean hydrogen,  $C_1$ - $C_{10}$ -alkyl, aryl,

C<sub>7</sub>-C<sub>20</sub>-aralkyl, or together a -(CH<sub>2</sub>)<sub>q</sub> group,

o means 2 to 4,

q means 3 to 6,

R<sup>20</sup> means OPG<sup>3</sup>, NHR<sup>29</sup>, or N<sub>3</sub>,

Z means an oxygen atom or H/OR<sup>12</sup>,

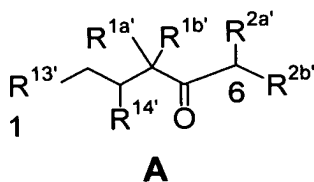
whereby

R<sup>12</sup> is hydrogen or a protective group PG<sup>Z</sup>

including all stereoisomers as well as mixtures thereof, and

free hydroxyl groups in R<sup>13</sup> and R<sup>14</sup> can be etherified or esterified, free carbonyl groups in Z and R<sup>13</sup> can be ketalized, converted into an enol ether or reduced, and free acid groups in R<sup>13</sup> and R<sup>14</sup> can be converted into their salts with bases, characterized in that

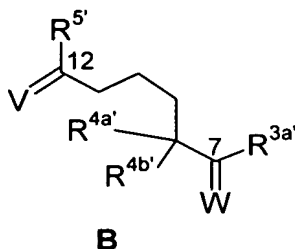
a C<sub>1</sub>-C<sub>6</sub> fragment (epothilone numbering system) of general formula A



in which

R<sup>1a'</sup>, R<sup>1b'</sup>, R<sup>2a'</sup>, R<sup>2b'</sup>, R<sup>13'</sup> and R<sup>14'</sup> have the meanings already mentioned for R<sup>1a</sup>, R<sup>1b</sup>, R<sup>2a</sup>, R<sup>2b</sup>, R<sup>13</sup> and R<sup>14</sup>, including all stereoisomers as well as mixtures thereof, and free hydroxyl groups in R<sup>13</sup> and R<sup>14</sup> can be etherified or esterified, free

carbonyl groups in A and  $R^{13}$  can be ketalized, converted into an enol ether or reduced, and free acid groups in A can be converted into their salts with bases, is reacted with a C7-C12 fragment (epothilone numbering system) of general formula



in which

$R^{3a\prime}$ ,  $R^{4a\prime}$ ,  $R^{4b\prime}$  and  $R^{5\prime}$  have the meanings already mentioned for  $R^{3a}$ ,  $R^4$  and  $R^5$ , and

V means an oxygen atom, two alkoxy groups  $OR^{17}$ , a  $C_2$ - $C_{10}$ -alkylene- $\alpha,\omega$ -dioxy group, which can be straight-chain or branched, or H/ $OR^{16}$ ,

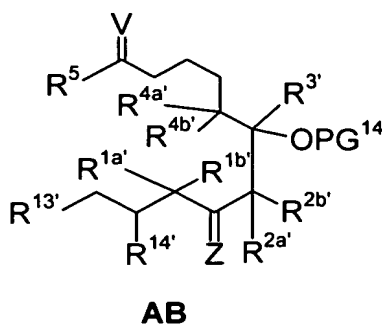
W means an oxygen atom, two alkoxy groups  $OR^{19}$ , a  $C_2$ - $C_{10}$ -alkylene- $\alpha,\omega$ -dioxy group, which can be straight-chain or branched, or H/ $OR^{18}$ ,

$R^{16}$ ,  $R^{18}$ , independently of one another, mean hydrogen or a protective group

$PG^1$ ,

$R^{17}$ ,  $R^{19}$ , independently of one another, mean  $C_1$ - $C_{20}$ -alkyl,

to form a partial fragment of general formula AB

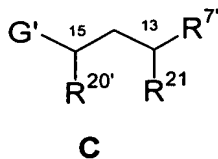


in which

$R^{1a'}$ ,  $R^{1b'}$ ,  $R^{2a'}$ ,  $R^{2b'}$ ,  $R^{3'}$ ,  $R^{4a'}$ ,  $R^{4b'}$ ,  $R^5$ ,  $R^{13'}$ ,  $R^{14'}$ ,  $V$  and  $Z$  have the already-mentioned meanings, and

$PG^{14}$  represents a hydrogen atom or a protective group PG, and

this partial fragment of general formula AB is reacted with a C13-C15 fragment (epothilone numbering system) of general formula C



in which

$G'$  has the meaning already mentioned in general formula I for G, and

$R^{7'}$  means a hydrogen atom,

$R^{20'}$  means halogen,  $N_3$ ,  $NHR^{29}$ , a hydroxy group, a protected hydroxy group

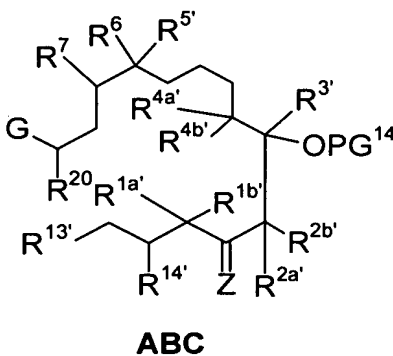
$O-PG^3$ , a protected amino group  $NR^{29}PG^3$ , a  $C_1$ - $C_{10}$ -alkylsulfonyloxy

group, which optionally can be perfluorinated, a benzyloxy group that is optionally substituted by C<sub>1</sub>-C<sub>4</sub>-alkyl, nitro, chlorine or bromine, an NR<sup>29</sup>SO<sub>2</sub>CH<sub>3</sub> group, an NR<sup>29</sup>C(=O)CH<sub>3</sub> group, or a CH<sub>2</sub>-C(=O)-CH<sub>3</sub> group,

R<sup>21</sup> means a hydroxy group, halogen, a protected hydroxy group OPG<sup>3</sup>, a phosphonium halide radical PPh<sub>3</sub><sup>+</sup>Hal<sup>-</sup> (Ph = Phenyl; Hal = F, Cl, Br, I), a phosphonate radical P(O)(OQ)<sub>2</sub> (Q = C<sub>1</sub>-C<sub>10</sub>-alkyl or phenyl) or a phosphine oxide radical P(O)Ph<sub>2</sub> (Ph = Phenyl),

R<sup>29</sup> means hydrogen or C<sub>1</sub>-C<sub>6</sub>-alkyl,

to form a compound of general formula ABC (= compound of general formula I)



in which

R<sup>1a'</sup>, R<sup>1b'</sup>, R<sup>2a'</sup>, R<sup>2b'</sup>, R<sup>3'</sup>, R<sup>4a'</sup>, R<sup>4b'</sup>, R<sup>5'</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>13</sup>, R<sup>14</sup>, G and Z have the already mentioned meanings, and

PG<sup>14</sup> represents a hydrogen atom or a protective group PG.

2. Process according to claim 1, wherein a compound of general formula I,  
in which

$R^{1a}$ ,  $R^{1b}$  are the same and mean  $C_1$ - $C_6$ -alkyl, or together mean a  $-(CH_2)_m$  group

with  $m = 2, 3$  or  $4$ ,

$R^{2a}$ ,  $R^{2b}$  are different and mean hydrogen,  $C_1$ - $C_6$ -alkyl,  $C_2$ - $C_{10}$ -alkenyl,

$C_2$ - $C_{10}$ -alkinyl or  $C_7$ - $C_{20}$ -aralkyl,

$R^5$  means hydrogen,  $C_1$ - $C_6$ -alkyl,

$R^8$  means hydrogen, halogen,  $C_1$ - $C_6$ -alkyl,

$R^{15a}$ ,  $R^{15b}$  are the same or different and mean hydrogen,  $C_1$ - $C_6$ -alkyl, aryl,

$C_7$ - $C_{20}$ -aralkyl, or together mean a  $-(CH_2)_q$  group,

$q$  means  $3$  to  $6$ ,

is produced.

3. Process according to claim 1, wherein a compound of general formula I,  
in which

$R^{1a}$ ,  $R^{1b}$  are the same and mean  $C_1$ - $C_3$ -alkyl, or together mean a  $-(CH_2)_m$  group

with  $m = 2, 3$  or  $4$ ,

$R^{2a}$  means hydrogen,

$R^{2b}$  means  $C_1$ - $C_5$ -alkyl,  $C_2$ - $C_6$ -alkenyl, or  $C_2$ - $C_6$ -alkinyl,

$R^5$  means hydrogen, or  $C_1$ - $C_3$ -alkyl,

$R^6$ ,  $R^7$  together mean an additional bond,

$G$  means a group  $X=CR^8$ -, or a bicyclic aryl radical,

$R^8$  means hydrogen, fluorine, chlorine, or  $C_1$ - $C_3$ -alkyl,

$X$  means oxygen or a group  $CR^{10}R^{11}$ ,

$R^{10}$  means hydrogen,

$R^{11}$  means aryl,

$R^{13}$  means  $CH_2OR^{13a}$  or  $CO_2R^{13b}$ ,

$R^{14}$  means  $OR^{14a}$ ,

$R^{13a}$ ,  $R^{14a}$  together mean a  $CR^{15a}R^{15b}$  group,

$R^{13b}$  means hydrogen or  $C_1$ - $C_6$ -alkyl,

$R^{15a}$ ,  $R^{15b}$  are the same and mean  $C_1$ - $C_3$ -alkyl, or together mean a  $-(CH_2)_q$  group, or

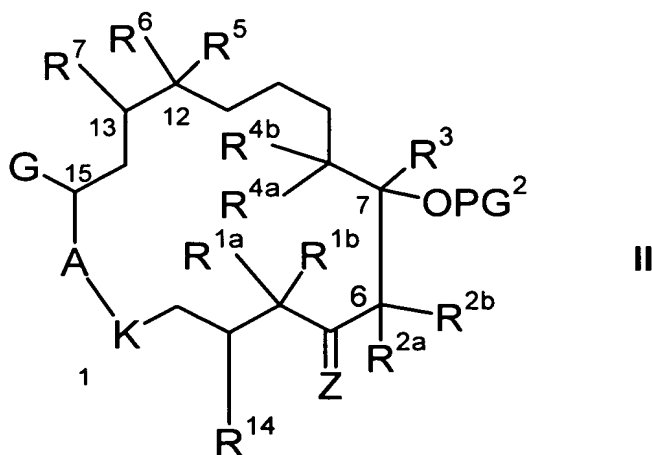
$R^{15a}$ ,  $R^{15b}$  are different and mean hydrogen or aryl,

$q$  means 4 or 5,

$Z$  means oxygen,

is produced.

#### 4. Process for the production of epothilone derivatives of general formula II

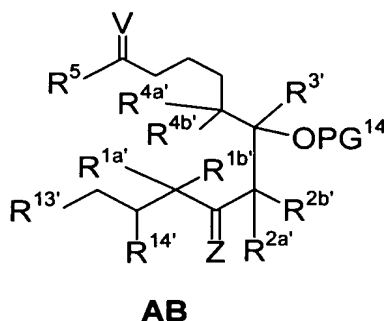




in which substituents  $R^{1a}$ ,  $R^{1b}$ ,  $R^{2a}$ ,  $R^{2b}$ ,  $R^3$ ,  $R^{4a}$ ,  $R^{4b}$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $G$ ,  $OPG^2$  and  $Z$  have the meanings that are indicated in general formula I, and

A–K means a group  $-O-C(=O)-$ ,  $-OCH_2-$ ,  $-CH_2C(=O)-$ ,  $-NR^{29}-C(=O)-$ , or  $-NR^{29}-SO_2-$ , wherein an initial epothilone product of general formula I that is obtained according to one of the preceding claims 1 to 3 is cyclized.

#### 5. Compounds of general formula AB



in which  $R^{1a'}$ ,  $R^{1b'}$ ,  $R^{2a'}$ ,  $R^{2b'}$ ,  $R^{3'}$ ,  $R^{4a'}$ ,  $R^{4b'}$ ,  $R^5$ ,  $R^{13'}$ ,  $R^{14'}$ ,  $V$  and  $Z$  have the already mentioned meanings, and  $PG^{14}$  represents a hydrogen atom or a protective group  $PG$ .